

(12) **UK Patent Application** (19) **GB** (11) **2 302 651** (13) **A**

(43) Date of Printing by UK Office 29.01.1997

(21) Application No 9624252.4

(22) Date of Filing 22.03.1995

(86) International Application Data  
PCT/JP95/00526 En 22.03.1995

(87) International Publication Data  
WO96/29062 En 26.09.1996

(71) Applicant(s)  
Teikoku Seiyaku Kabushiki Kaisha  
  
(Incorporated in Japan)

567 Sanbonmatsu, Ouchi-cho, Okawa-gun,  
Kagawa-ken, Japan

(72) Inventor(s)  
Akihito Oji  
Takashi Mizobuchi

(51) INT CL<sup>6</sup>  
A61K 9/70, A61F 7/02, A61K 31/045

(52) UK CL (Edition O )  
A5B BJA BLD B170 B23Y B230 B232 B30Y B301 B31X  
B31Y B35Y B351 B40Y B402 B826  
U1S S2416

(56) Documents Cited by ISA  
JP 630135328 A JP 590027821 A JP 550045626 A

(58) Field of Search by ISA  
INT CL<sup>6</sup> A61F 7/02, A61K 9/70 31/045

(74) Agent and/or Address for Service  
Mewburn Ellis  
York House, 23 Kingsway, LONDON, WC2B 6HP,  
United Kingdom

(54) Cold sheet

(57) A cold patch excellent in the persistence of the cooling effect, prepared by adding l-methanol and ethanol to a plaster composition containing a water-soluble high-molecular-weight substance, a polyhydric alcohol and water in a weight ration of 1/0.5 to 1/10.

GB 2 302 651 A

## COLD SHEET

## TECHNICAL FIELD OF THE INVENTION

The present invention relates to a cold patch, called a "cold sheet", and more particularly, to a patch excellent in the persistence of the cooling effect which comprises a paste composition comprising a water-soluble high-molecular-weight substance, a polyhydric alcohol and water, said composition being incorporated with l-menthol and ethanol for providing the cooling effect.

## TECHNICAL BACKGROUND

Hitherto, a patch has widely been used for the purpose of suppressing a blood flow and for relieving pain at a local inflammation with fever such as bruise, contusion, etc. For this purpose, it is desired that a patch not only has physiological properties such as a good adhesion to the skin and easiness of peeling from the skin without paste remaining on the skin but also efficiently provides the cooling effect persistently.

A patch has conventionally been prepared by mixing and blending kaolin, gelatin, glycerol, a water-soluble high-molecular-weight substance, water etc. with one or more active reagents such as methyl salicylate, ethylene glycol salicylate, dl-camphor, etc. and then applying this mixture to a support such as non-fabrics. Such a patch is supplemented with l-menthol as an essential component for providing the cooling effect. However, since l-menthol is an

oily substance which quite easily evaporates and the persistence of the cooling effect is not sufficient, there have been made various attempts to improve the persistence of the cooling effect. For example, there have been proposed a method wherein l-menthol is incorporated within cyclodextrin and a method wherein l-menthol is dispersed in a surfactant solution. However, even a patch prepared by these methods could not attain a sufficient persistence of the cooling effect. A patch with a large amount of water has also been known, which utilizes heat of vaporization when water vaporizes to promote the cooling effect at the affected part (Japanese Patent First Publication No. 54-106598, Japanese Patent First Publication No. 59-110615). Due to a high content of water in a base, this type of a patch exhibits a poor maintenance of shape and, at a season of much perspiration such as in summer, the water content in the base becomes too high due to perspiration at the applied part to induce so-called looseness and stickiness. Furthermore, due to difficulty in incorporating a humectant such as glycerol, propylene glycol, etc. into a base, this type of a patch is also disadvantageous in that water evaporates in a short period of time and thereby the persistence of the cooling effect still remains insufficient.

The present inventors have earnestly studied in order to obviate the above-mentioned disadvantages, and as a result, have found that the persistence of the cooling effect can be improved by incorporating l-menthol and ethanol at a

specific ratio into a paste composition comprising a water-soluble high-molecular-weight compound, a polyhydric alcohol and water, and thereby the present invention has been completed.

#### DISCLOSURE OF THE INVENTION

That is, a patch of the present invention is characterized by that 1-menthol and ethanol are incorporated as a reagent for providing the cooling effect at a specific ratio into a paste composition comprising a water-soluble high-molecular-weight compound, a polyhydric alcohol and water.

A water-soluble high-molecular-weight substance used herein includes gelatin, polyacrylic acid, sodium polyacrylate, polyvinyl alcohol, polyvinyl pyrrolidone, a carboxyvinyl polymer, sodium carboxymethyl cellulose, hydroxypropyl cellulose, methyl cellulose, ethyl cellulose, a methyl vinyl ether/maleic anhydride copolymer, sodium alginate, poly(ethylene oxide), acacia, glucomannan, xanthan gum, tragacanth gum, etc., or a mixture of one or more thereof. Although an amount of a water-soluble high-molecular-weight substance to be incorporated into a paste composition is not particularly limited, with less than 2% (% by weight, hereinafter the same) of the compound based on a whole amount of a paste composition, the composition does not have a sufficient viscosity and does not become a paste. On the other hand, where more than 20% of a water-soluble high-molecular-weight substance is incorporated into a paste

composition, a viscosity of the resulting composition is too high and thus it becomes difficult to handle during a production process. Accordingly, a water-soluble high-molecular-weight substance is incorporated into a paste composition at an amount ranging from 2 to 20%, preferably from 5 to 15%, based on a whole amount of the composition.

A polyhydric alcohol as used herein includes glycerol, sorbitol, propylene glycol, poly(ethylene glycol), 1,3-butylene glycol, ethylene glycol, etc. or a mixture of one or more thereof. An amount of a polyhydric alcohol to be incorporated into a paste composition ranges from 8 to 60%, preferably from 10 to 50%, based on a whole amount of the composition. Where the amount is less than 8%, a humectant effect is not sufficient and hence water evaporates in a short period of time, thereby the effects of 1-menthol and ethanol, i.e. the cooling effect, is not persistent for a long period of time. On the other hand, where the amount is more than 60%, an amount of other components to be incorporated into a paste composition is restricted.

Water is typically incorporated into a paste composition in an amount ranging from 20 to 80%, preferably from 25 to 70%, based on a whole amount of the composition. Where the amount is less than 20%, a solubility of a water-soluble high-molecular-weight substance is unacceptably lowered and hence a uniform spreading becomes impossible. On the other hand, where the amount is more than 80%, a paste

composition is too much softened and the resulting patch is apt to exhibit looseness.

A ratio of an amount of l-menthol and ethanol to be incorporated into a paste composition comprising a water-soluble high-molecular-weight substance, a polyhydric alcohol and water is preferably in a range from 1:0.5 to 1:10, more preferably from 1:1 to 1:5. Apart from this range, the cooling effect is not persistent. An amount of ethanol to be incorporated into a paste composition is preferably in a range from 0.1 to 10% based on a whole amount of the composition. Where more than 10% of ethanol is incorporated, it possibly irritates the skin at the applied part, whereas the cooling effect cannot be obtained with less than 0.1% of ethanol.

In addition to the above-mentioned components, the paste composition of the present invention may further be incorporated with various additives which are usually used for a conventional patch, including an inorganic material, a surfactant, a cross-linking agent, etc. such as kaolin, bentonite, titanium oxide and the like in a usual amount.

The paste composition of the present invention is prepared in a usual manner by blending the components. For example, 1 part of a water-soluble high-molecular-weight substance and 1 part of a polyhydric alcohol are dissolved in water, and after optionally adding another components, a solution of l-menthol in ethanol is added to the mixture. The resulting mixture is blended and further added with the remaining of a water-soluble high-molecular-weight substance

and other additives, and after blending, the paste composition of the present invention is prepared.

The thus prepared paste composition is then applied and spread onto a support cloth sheet in a usual manner, and the applied surface is covered with a releasing paper for protection, which is then cut into an appropriate size to produce a desired patch.

For a support cloth sheet, any material used for a conventional patch such as non-fabrics, textile, knitted material, etc. may be used. Such a support cloth sheet may be made of either synthetic or natural fibers such as nylon, rayon, polyester, polypropylene. A releasing paper may also be any one which is used for a usual patch including a plastic film such as a polyethylene film.

#### BEST MODE FOR CARRYING OUT THE INVENTION

The invention is more fully explained by means of Examples but should not be construed to be limited to the following Examples.

##### Example 1

[Component]	[% (W/W)]
Polyacrylic acid	6.0
Sodium polyacrylate	5.0
Sodium carboxymethyl cellulose	5.0
Gelatin	1.0
Polyvinyl alcohol	0.5
Tartaric acid	0.2
Glycerol	20.0

Aluminum hydroxide	0.5
Methylparaben	0.1
l-Menthol	0.6
Ethanol	0.5
<u>Purified water</u>	<u>the rest</u>
Total	100.0

To 15 parts of purified water are added gelatin and polyvinyl alcohol and the mixture is dissolved with heating. To this solution is added methylparaben and the mixture is well blended. To this mixture are then added a solution of l-menthol in ethanol, tartaric acid and the rest of purified water, and the mixture is further blended until homogeneity is obtained. Finally, a solution in which polyacrylic acid, sodium polyacrylate, sodium carboxymethyl cellulose and aluminum hydroxide are dispersed in glycerol is added to the mixture, which is well blended to produce a paste composition. The resulting paste composition is spread onto a support cloth sheet made of rayon fiber at 1000 g/m<sup>2</sup> and then the surface of the paste composition is covered with a plastic film, which is cut at an appropriate size to produce a patch.

Example 2

[Component]	[%(W/W)]
Sodium polyacrylate	4
Sodium carboxymethyl cellulose	3
Gelatin	2
Polyvinyl pyrrolidone	1



Glycerol	25
D-Sorbitol solution	20
Kaolin	5
Aluminum hydroxide	0.8
Tartaric acid	0.4
Methylparaben	0.1
Propylparaben	0.05
l-Menthol	1
Ethanol	0.5
Purified water	<u>the rest</u>
Total	100.0

To 15 parts of purified water are added gelatin and polyvinyl pyrrolidone and the mixture is dissolved with heating. To this solution are added methylparaben and propylparaben and the mixture is well blended. To this mixture are then added a solution of l-menthol in ethanol, tartaric acid, kaolin, D-sorbitol solution and the rest of purified water, and the mixture is further blended until homogeneity is obtained. Finally, a solution in which sodium polyacrylate, sodium carboxymethyl cellulose and aluminum hydroxide are dispersed in glycerol is added to the mixture, which is well blended to produce a paste composition. The resulting paste composition is spread onto a support cloth sheet made of polyester fiber at 1000 g/m<sup>2</sup> and then the surface of the paste composition is covered with a releasing paper, which is cut at an appropriate size to produce a patch.

Example 3

[Component]	[% (W/W)]
Polyacrylic acid	1
Sodium polyacrylate	2
Sodium alginate	3
Gelatin	1
Polyvinyl alcohol	0.5
Glycerol	16
Propylene glycol	10
Magnesium metasilicate aluminate	0.4
Propylparaben	0.05
Methylparaben	0.1
l-Menthol	3
Ethanol	9
<u>Purified water</u>	<u>the rest</u>
Total	100.0

To 15 parts of purified water are added gelatin and polyvinyl alcohol and the mixture is dissolved with heating. To this solution are added methylparaben and propylparaben and the mixture is well blended. To this mixture are then added a solution of l-menthol in ethanol and the rest of purified water, and the mixture is further blended until homogeneity is obtained. Finally, a solution in which polyacrylic acid, sodium polyacrylate, sodium alginate and magnesium metasilicate aluminate are dispersed in a mixture of glycerol and propylene glycol is added to the mixture, which is well blended to produce a paste composition. The resulting paste

composition is spread onto a support cloth sheet made of nylon fiber at 1000 g/m<sup>2</sup> and then the surface of the paste composition is covered with a releasing paper, which is cut at an appropriate size to produce a patch.

#### Comparative Example 1

The procedures in Example 1 are repeated except that 1-menthol is replaced with an equal amount of water to produce a patch.

#### Comparative Example 2

The procedures in Example 1 are repeated except that ethanol is not used and 1-menthol is replaced with an equal amount of liquid menthol calculated as 1-menthol to produce a patch.

#### Comparative Test 1

With the patches prepared in Examples 1, 2 and 3 and Comparative Examples 1 and 2, each ten test strips (7 cm x 10 cm) were prepared. Each one test strip was applied at random to the back of 25 subjects and the cooling effect was assessed 2 hours and 12 hours after application wherein the persistence of the cooling effect was also evaluated.

§ Cooling effect: feeling of cooling during application is evaluated based the following criteria.

- +: Feeling extensively cooling
- ±: Feeling cooling
- : Feeling no cooling

§ Persistence of the cooling effect: this is evaluated by reports from subjects of persistence of feeling cooling.

Table 1

	Cooling effect		Persistence of cooling effect <u>(Hour)</u>
	<u>2 hours</u>	<u>After</u> <u>12 hours</u>	
Example 1	+	±	12.0
Example 2	+	±	12.0
Example 3	+	±	12.0
Comp. Ex. 1	-	-	1.5
Comp. Ex. 2	±	-	2.4

As is evident from the above results, it was found that the patch of the present invention has excellent properties in the persistence of the cooling effect due to incorporation of 1-menthol and ethanol into a paste composition comprising a water-soluble high-molecular-weight substance.

CLAIMS

1. A cold patch which comprises a paste composition comprising a water-soluble high-molecular-weight substance, a polyhydric alcohol and water, said  
5 composition incorporating 1-menthol and ethanol at a weight ratio ranging from 1:0.5 to 1:10.
2. The cold patch of claim 1 wherein ethanol is incorporated in an amount ranging from 0.1 to 10% by weight based on a whole amount of the paste composition.
- 10 3. The cold patch of claim 1 wherein said patch comprises 2 to 20% by weight of the water-soluble high-molecular-weight substance, 8 to 60% by weight of the polyhydric alcohol, 20 to 80% by weight of water, 0.1 to 5% by weight of 1-menthol and 0.1 to 10% by weight of  
15 ethanol.
4. A cold patch substantially as herein described.
5. A paste composition for use in the preparation of a cold patch according to any one of the preceding claims, the composition comprising a water-soluble high-  
20 molecular-weight substance, a polyhydric alcohol and water, and further incorporating 1-menthol and ethanol at a weight ratio of between 1:0.5 and 1:10.

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/JP95/00526

## A. CLASSIFICATION OF SUBJECT MATTER

Int. Cl<sup>6</sup> A61K9/70, 31/045, A61F7/02

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Int. Cl<sup>6</sup> A61K9/70, 31/045, A61F7/02

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	JP, 59-27821, A (Kanebo, Ltd.), February 14, 1984 (14. 02. 84) (Family: none)	1 - 3
A	JP, 55-45626, A (Lion Corp.), March 31, 1980 (31. 03. 80) (Family: none)	1 - 3
A	JP, 63-135328, A (Kao Corp.), June 7, 1988 (07. 06. 88) (Family: none)	1 - 3

☐ Further documents are listed in the continuation of Box C.☐ See patent family annex.

## \* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, each combination being obvious to a person skilled in the art

"A" document member of the same patent family

Date of the actual completion of the international search

May 22, 1995 (22. 05. 95)

Date of mailing of the international search report

June 13, 1995 (13. 06. 95)

Name and mailing address of the ISA/

Japanese Patent Office

Authorized officer

Facsimile No.

Telephone No.